

In Vivo Cancer Studies

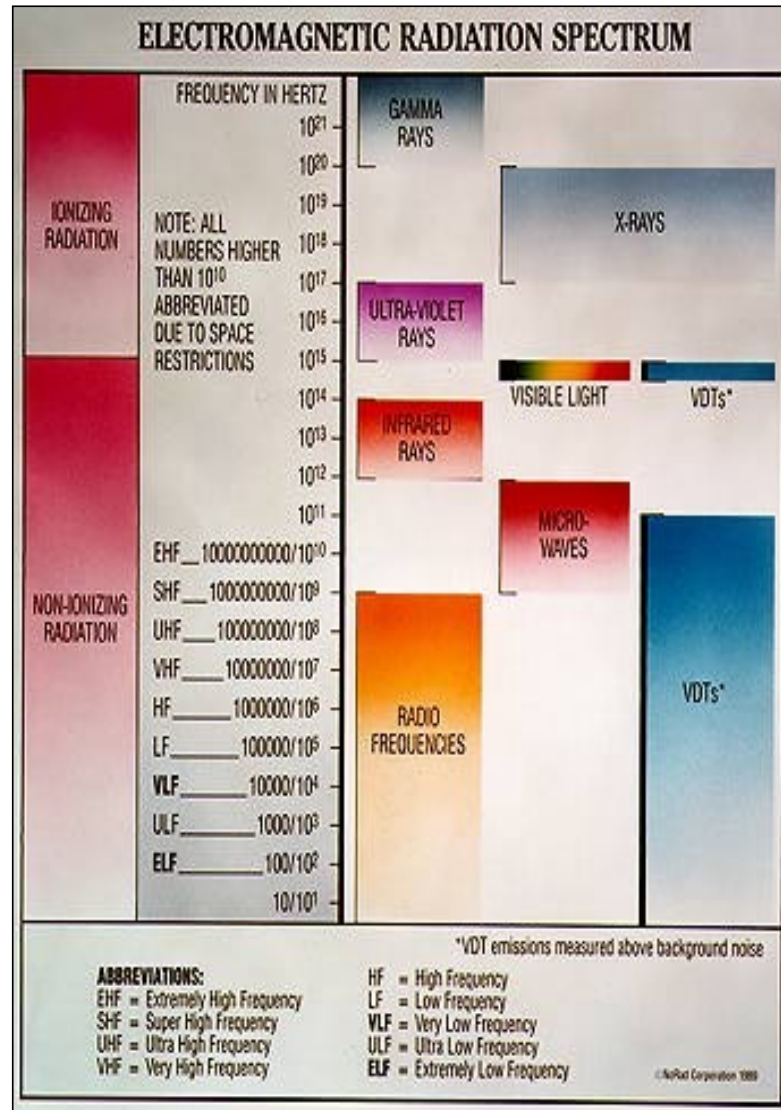
18 April 2002

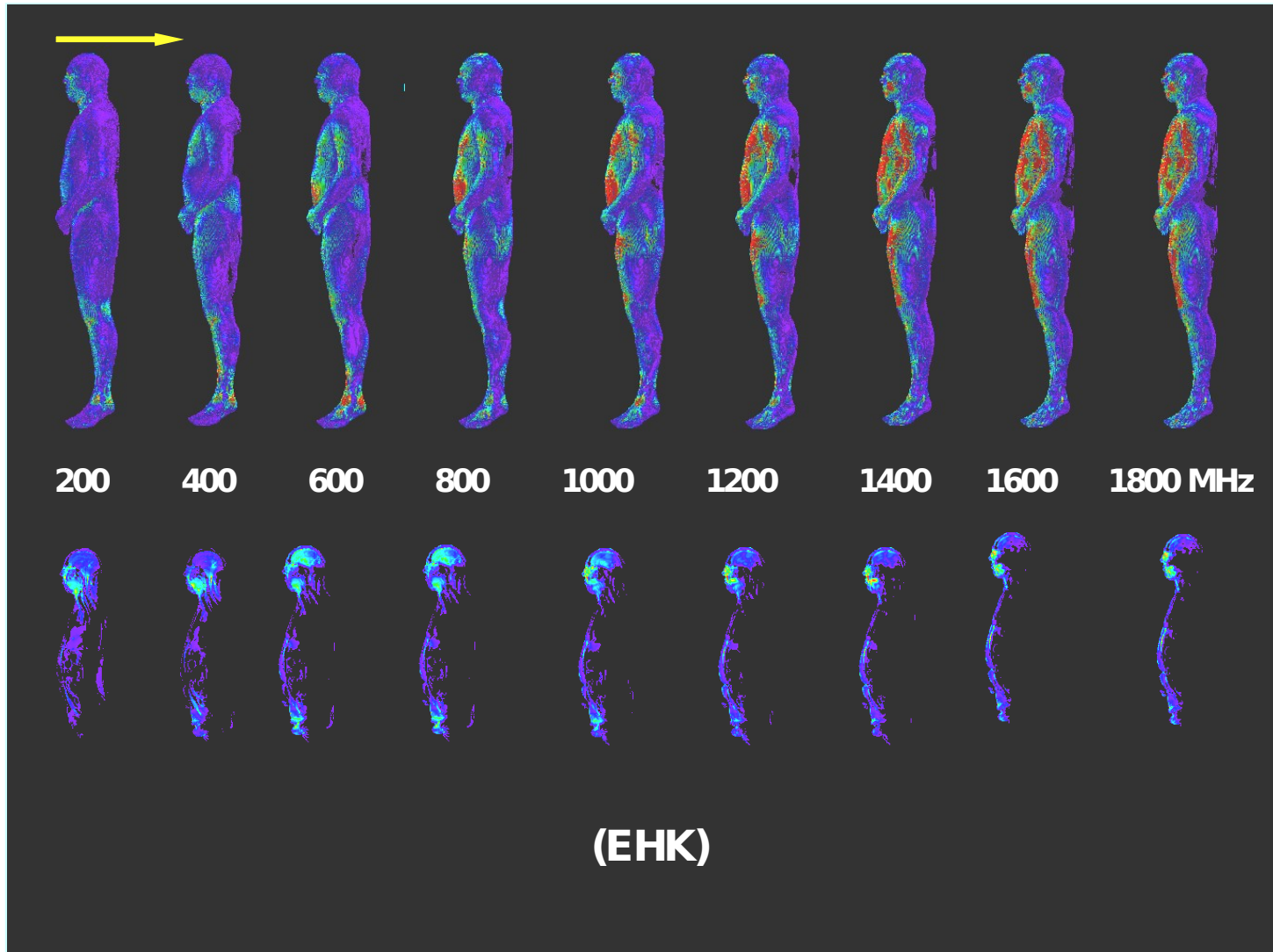


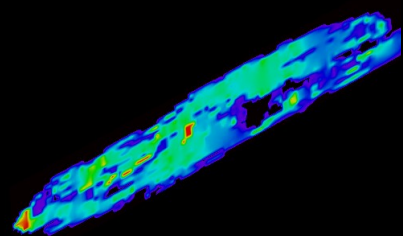
Patrick Mason, Ph.D.
Research Physiologist
Human Effectiveness
Directorate
Air Force Research
Laboratory



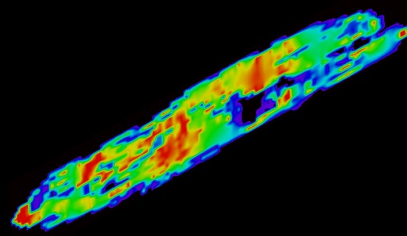
Background



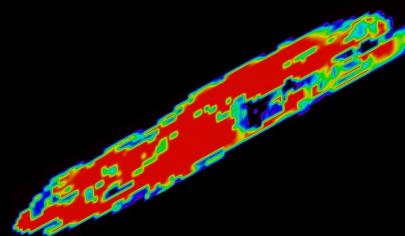




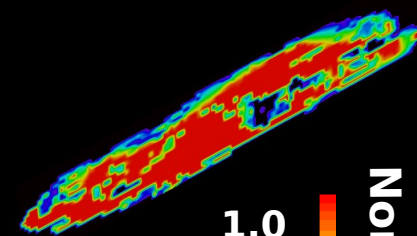
300



400



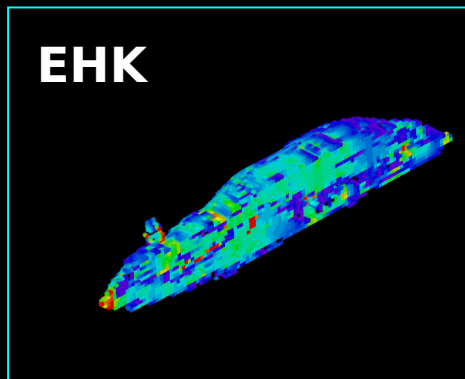
500



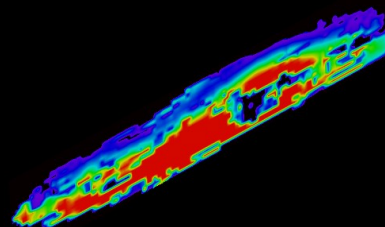
1.0

600

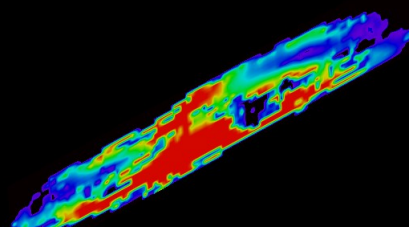
Normalized SAR (W/kg/mW/cm^2)



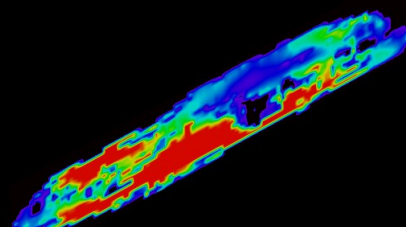
EHK



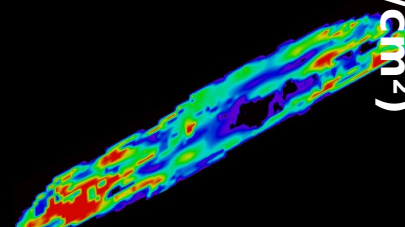
700



900



1100



2060 MHz



**Szmigielski, S. Szudzinski, A.,
Pietraszek, A., Bielec, M., Janiak, M.,
and Wrembel, J.K.**

**Szudzinski, A., Pietraszek, A., Janiak,
M., Wrembel, J., Kalczak, M., and
Szmigielski, S.**

**Centre for Radiobiology and
Radioprotection,
Warsaw, Poland**



Mammary Cancer and Skin Cancer - 2450 MHz

C3H/HeA mice (mammary tumors) or Balb/c mice painted with 3,4-benzopyrene.

Exposed to 2450 MHz (5 - 15 mW/cm², 2 - 8 mW/kg), 2 hours/day, 6 days/week, 1-6 months.

RESULTS: Microwave exposure decreased latency of tumor onset. Similar results were obtained in animals exposed to chronic, confinement stress. Suggest microwave results could be due to a nonspecific stress reaction.

Szmigielski, S.; Szudzinski, A.; Pietraszek, A.; Bielec, M.; Janiak, M.; Wrembel, J. K. Accelerated development of spontaneous and benzopyrene-induced skin cancer in mice exposed to 2450-MHz microwave radiation. Bioelectromagnetics 3:179-191; 1982.

Szudzinski, A.; Pietraszek, A.; Janiak, M.; Wrembel, J.; Kalczak, M.; Szmigielski, S. Acceleration of the development of benzopyrene induced skin cancer in mice by microwave



**Santini, R., Hosni, M., Deschaux, P.,
and Pacheco, H.**

**Laboratoire de Physiologie
Pharmacodynamie, Limoges, France**



B16 Melanoma Formation



C57/6J mice with B16 melanoma

2450 MHz, 1.2 mW/g, continuous wave (1 mW/cm² or **pulsed fields (10 microsecond pulse duration, 5 microsecond interpulse interval), 2.5 hours/day, 6 sessions/week for up to 690 hours of exposure**

RESULTS: No significant difference between exposed and control animals in tumor development or survival times.

No significant difference between animals exposed to continuous wave or pulsed fields.

Santani *et al.*, B16 melanoma development in black mice exposed to low-level microwave radiation



**C.K. Chou, A.W. Guy, L.L. Kunz,
R.B. Johnson, J.J. Crowley, and J.H.
Krupp**

University of Washington

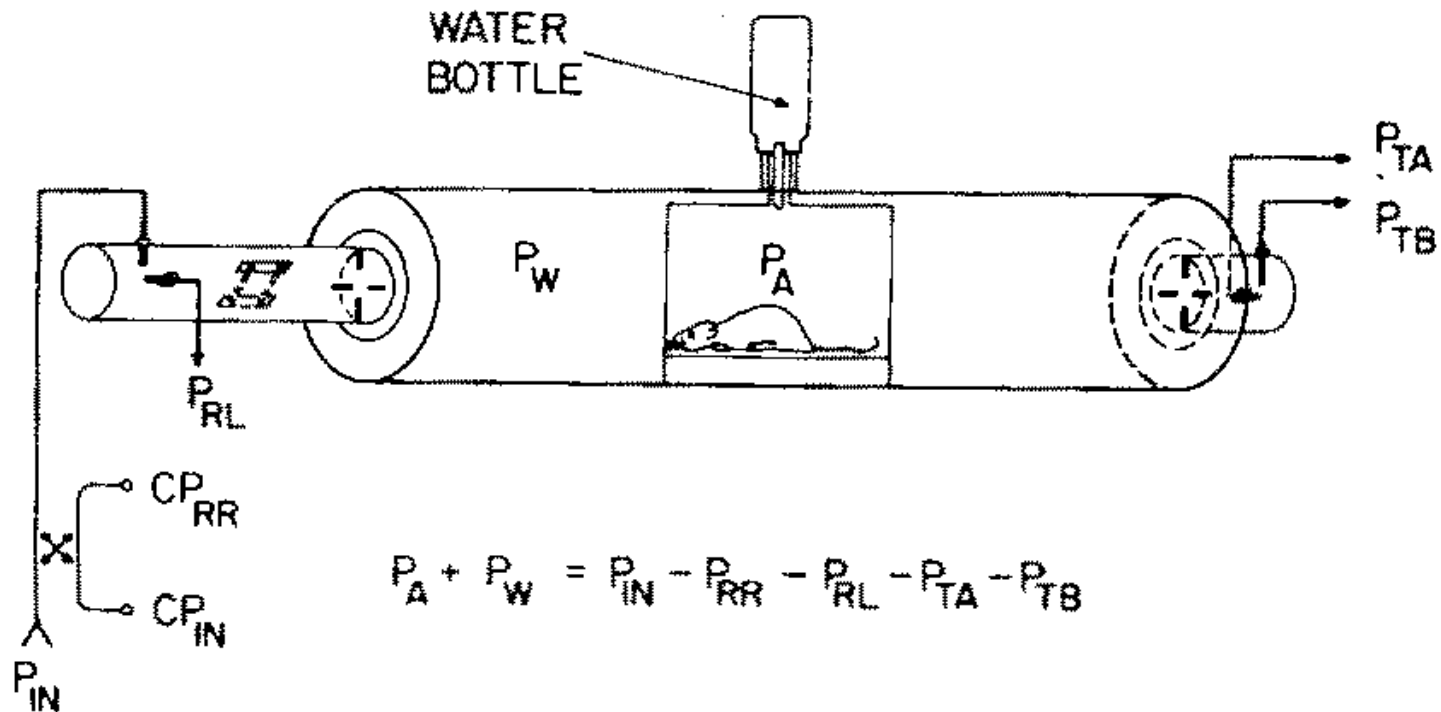


Methods

- **200 male Sprague-Dawley rats**
 - **100 exposed; 100 sham-exposed**
- **Circularly-polarized waveguides**
 - **2450 MHz, pulsed (10 microsecond, 800 pps)**
 - **SAR = 0.4 W/kg (for 200 g rat) (1 mW/cm²)**
- **Exposure**
 - **21.5 hours/day, 7 days/week**
 - **25 months**



Circular Waveguide





Results



- Behavior **NS**
- Serum corticosterone **NS**
- Immunology **NS**
- Hematology **NS**
- Blood chemistry **NS**
- Urinalysis **NS**
- Metabolism **NS**
- Total body analysis **NS**
- Organ mass **NS**
- Longevity **NS**

SUMMARY: Results indicated no definitive, biologically significant effects.

**Chou et al., Long-term, low-level microwave irradiation of rats.
Bioelectromagnetics 13: 469-496, 1992**



Brain Glioma Formation



**Salford, L.G., Brun, A., Persson, B.R.R.,
and Eberhardt, J.**

**Salford, L.G., Brun, A., and Persson,
B.R.R.**

Lund University, Sweden



Brain Glioma Formation



Fischer 344 rats (males and females), 150 - 250 gm

5000 RG2 cells (rat glioma cell line) or N32 cells (rat glioma cell line - slow growth) injected into the caudate nucleus

915 MHz (continuous wave or modulated (4, 8, 16, 200 Hz in 0.5 ms **pulses) (.0077 - 1.67 W/kg). Exposed for 7 hours/day, 5 days/week for 2 - 3 weeks.**

RESULTS:

- No significant difference between exposed and sham animals.**
- No significant difference between animals exposed to continuous wave and modulated**



Salford et al., Experimental studies of brain tumor development during exposure to continuous and pulsed 915 MHz radiofrequency radiation. *Bioelectrochemistry and Bioenergetics*, 30: 313-318, 1993.

Salford et al., Brain tumour development in rats exposed to electromagnetic fields used in wireless cellular communications. *Wireless Networks*, 3: 463-469, 1997.



Mammary Tumor Formation



**J.C. Toler, W.W. Shelton, M.R.
Frei, J.H. Merritt, and M.A.
Stedham**

Georgia Tech Institute of Technology



Methods



- **400 female C3H/HeJ mice (Mammary tumor model recommended by National Cancer Institute)**
 - spontaneous mammary gland tumors
 - 200 Exposed, 200 Sham-exposed
- **Parallel-plate waveguides**
 - 435 MHz, **pulsed** (Designed to simulate PAVE PAWS)
 - SAR = 0.32 W/kg
- **Exposure**
 - 22 hours/day, 7 days/week
 - 21 months





Results

- **Animal Weights** **NS**
- **Survival Time** **NS**
- **Latency to tumor onset** **NS**
- **Mammary tumor growth rates** **NS**
- **Histopathology**
 - **Mammary tumors** **NS**

Toler JC, *et al.* Long-term, low-level exposure of mice prone to mammary tumors to 435-MHz radiofrequency radiation. *Radiat Res.* 148, 227-234 (1997)



**M.R. Frei, R.E. Berger, S.J. Dusch, V. Guel,
J.R. Jauchem, J.H. Merritt, and M.A.
Stedham**

**M.R. Frei, J.R. Jauchem, S.J. Dusch, J.H.
Merritt,
R.E. Berger, and M. Stedham**

Trinity University, San Antonio, TX



Methods

- **200 female C3H/HeJ mice**
 - **100 exposed, 100 sham-exposed**
- **Circularly polarized waveguides**
 - **2450 MHz, CW (Frequency of 2450 MHz allowed maximum absorption of energy in mouse)**
 - **SAR**
 - **CWG 1: 0.3 W/kg (1998a study)**
 - **CWG 2: 1.0 W/kg (1998b study)**
- **Exposure**
 - **20 hours/day, 7 days/week**
 - **18 months**





Endpoints



- **Animal weights**
- **Survival Time**
- **Latency to Tumor Onset**
- **Mammary Tumor Growth Rates**
- **Histopathology (34 tissues)**





Results (0.3 and 1.0 W/kg)



- Animal weights **NS**
- Survival Time **NS**
- Latency to Tumor Onset **NS**
- Mammary Tumor Growth Rates **NS**

Frei MR, et al. Chronic exposure of cancer-prone mice to low-level 2450-MHz radiofrequency radiation. *Bioelectromagnetics* 19, 20-31 (1998)

Frei MR, et al. Chronic, low-level (1.0 W/kg) exposure of mice prone to mammary tumors to 2450-MHz microwaves. *Radiat. Res.* 150, 568-576 (1998)



**Adey, W.R., Byus, C.V., Cain, C.D.,
Higgins, R.J., Jones, R.A., Kean, C.J.,
Kuster, N., MacMurray, A., Stagg, R.B.,
Zimmerman, G., Phillips, J.L., and
Haggren, W.**

University of California at Riverside

Loma Linda University



836 MHz **pulsed field, 1.8 - 2.3 W/kg.**

Fischer344 rats exposed on gestation days 19-21. Offspring exposed for 22 months, 4 days/week, 2 hours/day.

RESULTS: No significant difference in spontaneous or nitrosourea-induced primary tumor formation in exposed and control animals.

Adey *et al.*, Spontaneous and Nitrosourea-Induced Primary Tumors of the Central Nervous System in Fisher 344 Rats Chronically Exposed to 836 MHz Modulated Microwaves. Radiation Research, 152: 293-302, 1999.



Chagnaud, J.L., Moreau, J-M., and Veyret, B.

University of Bordeaux, France



Sprague-Dawley rats injected subcutaneously with benzo(a)pyrene.

Exposed to 900-MHz (55 to 220 microwatt/cm²) (75 to 270 mW/kg) for 2 hours/day, 5 days/week for 2 weeks.

RESULTS: No significant difference in tumor development between exposed and control animals. No acceleration or delays in tumor onset. Animal survival was not affected.

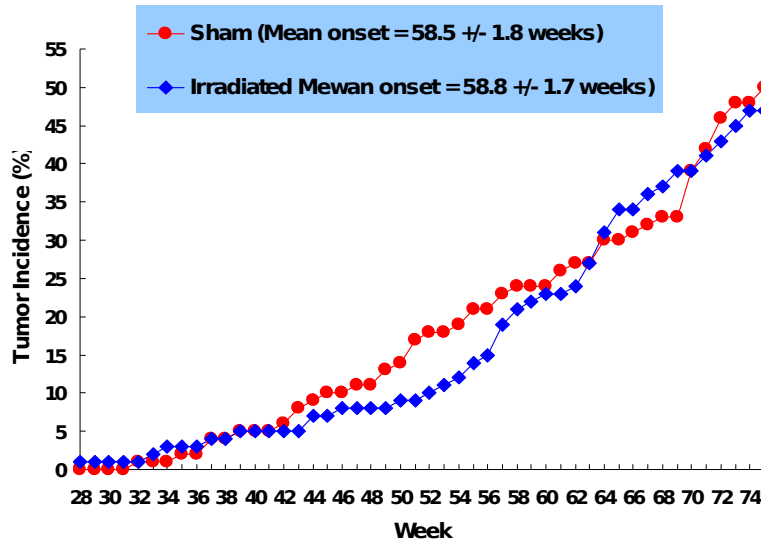
Chagnaud *et al.*, No effect of short-term exposure to GSM-modulated low power microwaves on benzo(a)pyrene-induced tumors in rat. *Int. J. Radiat. Biol.* 75: 1251-1256, 1999.



Ultrawide Band Cancer Study



- C3/HeJ mouse mammary tumor model
- Exposure:
 - Peak E-field = 40 kV/m; 300 ps pulse rise time; 1.8 ns pulse width, 1 kHz pulse rate, dominant freq range = .1 - 1 GHz
 - 2 min per day; 1 day per week for 16 weeks
- Measurements:
 - animal weight
 - latency to tumor appearance
 - tumor size
 - survival time
 - histopathology
- No significant effects
- Jauchem et al., *Radiation Research*, 155: 369-377, 2001





Ultrawide Band Bioeffects Studies

Teratology Study



Will UWB exposure affect fetal growth and development?

Kentech Exposure



Dams exposed 6m/day, day 3-18 gest;
Peak E-field = 55 kV/m; rise time = 300 ps; 1.8 ns pulse width; pulse rate = 1 kHz;

Dominant frequency range

= 0.1 - 1 GHz; 0.45 mJ/kg per pulse

- Pups examined for:
 - Air righting
 - Coat appearance
 - Eye opening
 - Tooth eruption
 - Growth rate
 - Locomotor behavior
 - Food consumption
 - Reproductive capability, frequency
 - Vocalizations
 - Hippocampal morphology (10 measures)

- 43 comparisons made

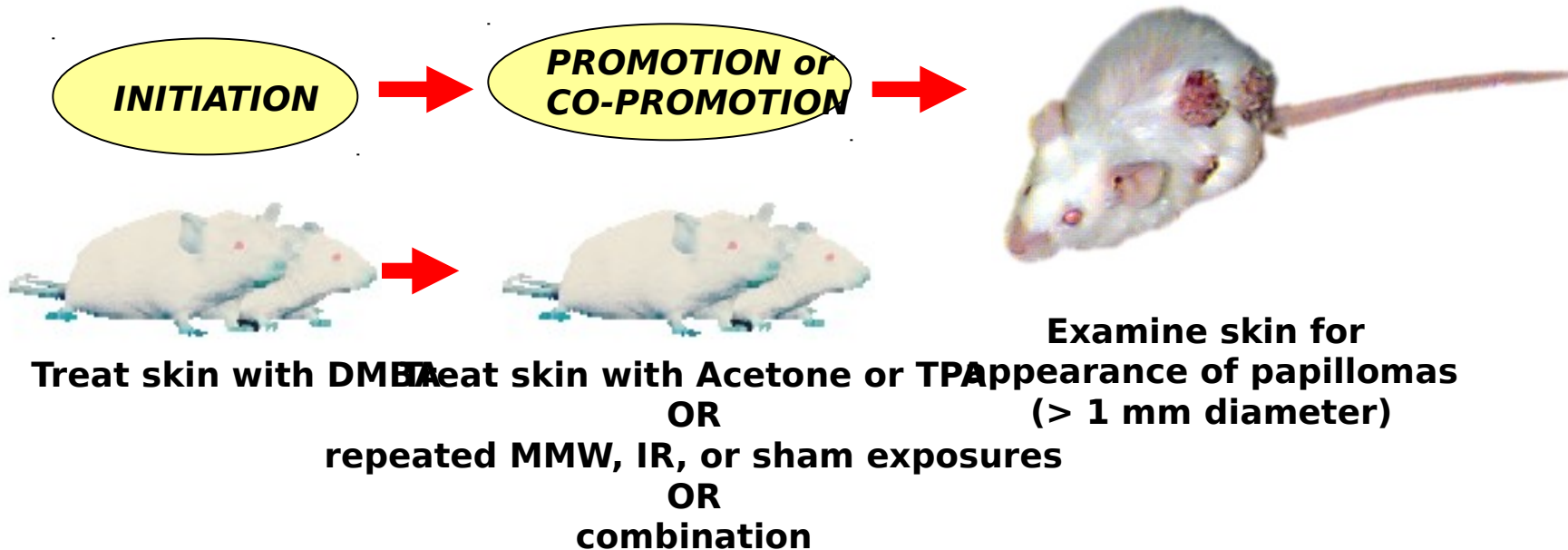
between sham & UWB

- Vocalization frequency increased

obb et al., *Bioelectromagnetics* 21:1, 2000

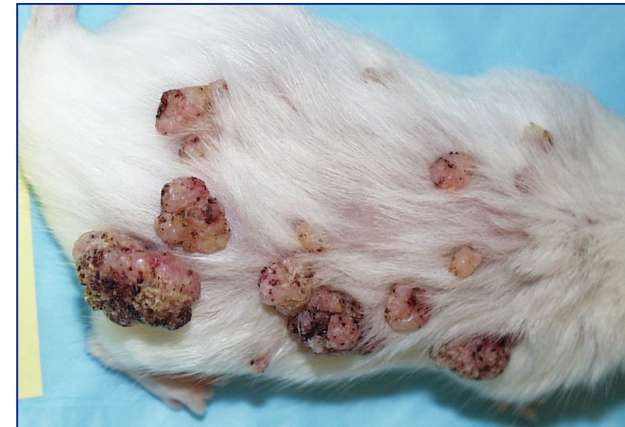


Do **REPEATED** millimeter wave exposures promote or co-promote skin cancer?



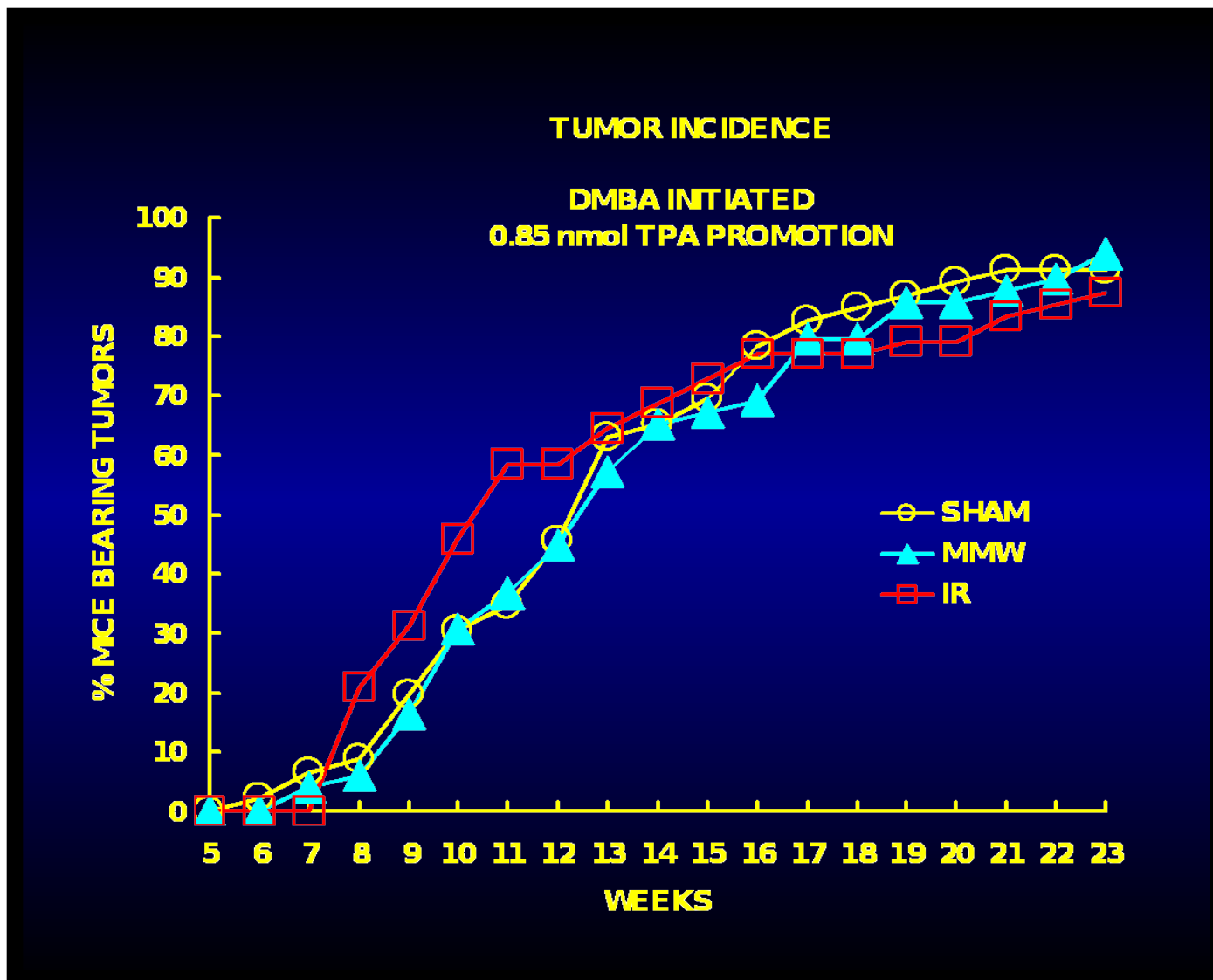


- **50 SENCAR mice/group**
- **7,12-dimethylbenz[a]anthracene (DMBA) induced. Acetone or 12-O-tetradecanoylphorbol-13-acetate (TPA) promotion (0.85 nmoles) two times/week throughout experiment (23 weeks)**
- **Exposures**
 - **2 times/week for 12 weeks**
 - **333 mW/cm² for 10 sec**
 - **Skin temperature increased 4**



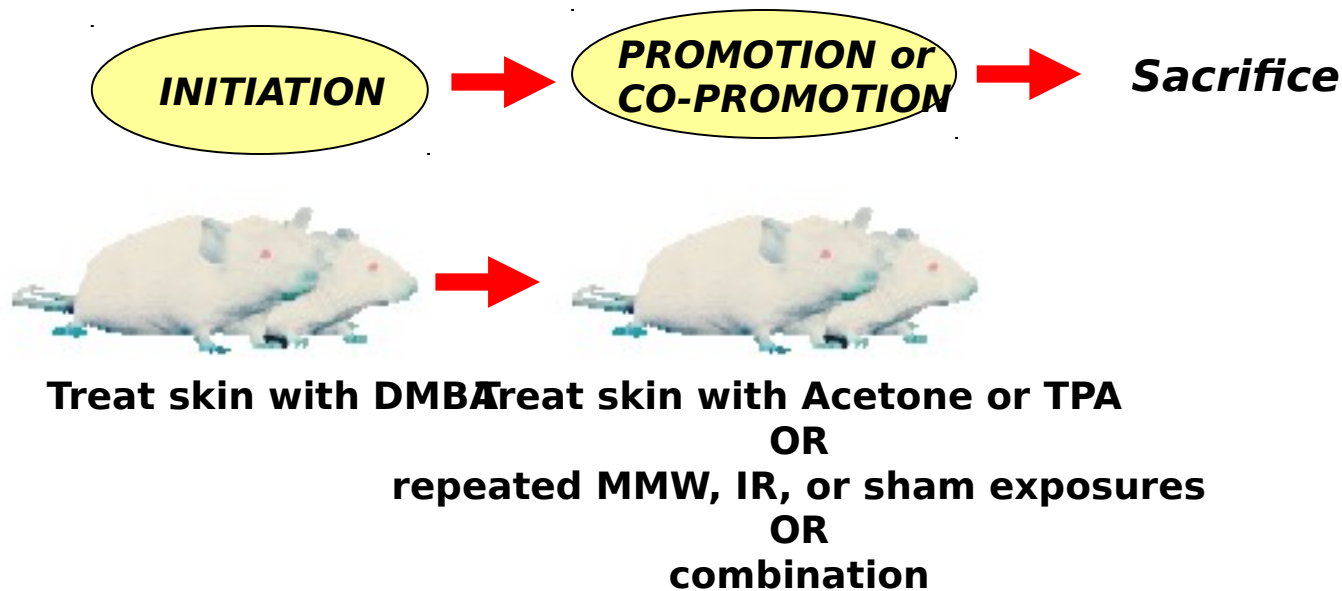


EXPERIMENT 2 - TUMOR INCIDENCE (TPA co-promotion)





Are short-term biomarkers for promotion/co-promotion altered by **REPEATED** exposures?





- **4 animals euthanized at each of 1, 2 and 5 weeks following start of TPA promotion**
- **Examined:**
 - **Epidermal thickness**
 - **Epidermal Bromodeoxyuridine (BrdUrd) labeling**
 - **Epidermal Ornithine decarboxylase (ODC) activity**

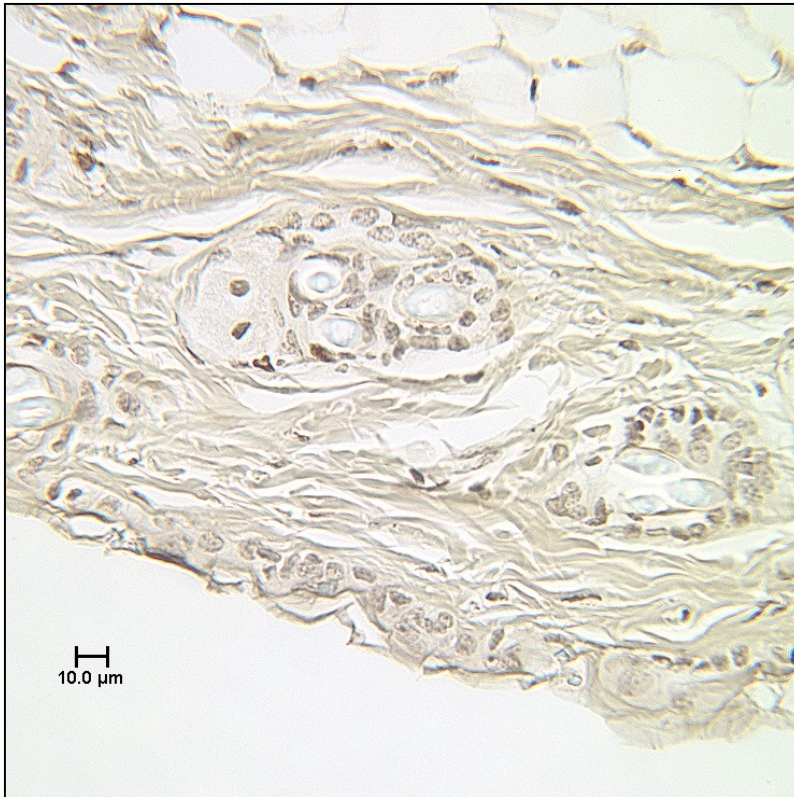


BrdUrd is an analogue of the DNA base thymidine. Only those cells that have been actively synthesising DNA during the time that BrdUrd is present will be positive for it.

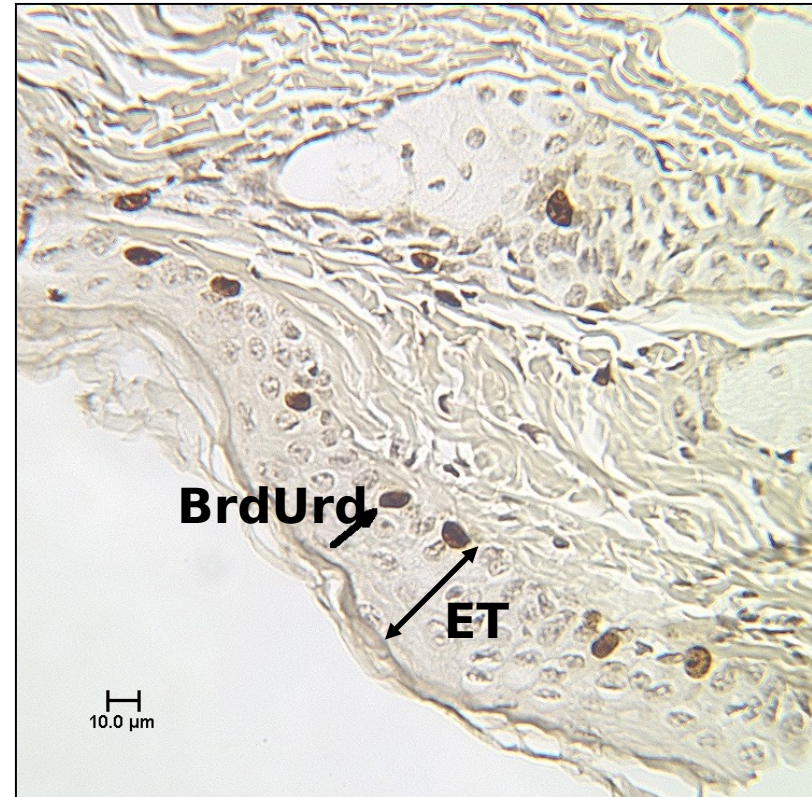
ODC is a key enzyme in the biosynthesis of polyamines that promote cell proliferation.



5-bromodeoxyuridine (BrdUrd) Epidermal Thickness (ET)



- DMBA
- Sham
- Acetone



- DMBA
- Sham
- TPA (0.85 nmol)



CONCLUSION

MMW exposure under these experimental conditions does not promote or co-promote tumorigenesis in this well-established animal model of skin carcinogenesis.

Mason *et al.*, Lack of effect of 94 GHz radio frequency radiation exposure in an animal model of skin carcinogenesis. *Carcinogenesis*, 22: 1701-1708, 2001.

- Consultant

–John DiGiovanni, Ph.D. (University of Texas M.D. Anderson Cancer Center)



**Imada, K., Juzutani, K., Wang, J.,
Fujiwara, O., Ogiso, T., Kato, K.,
and Shirai, T.**

**Nagoya City University Medical
School, Japan**

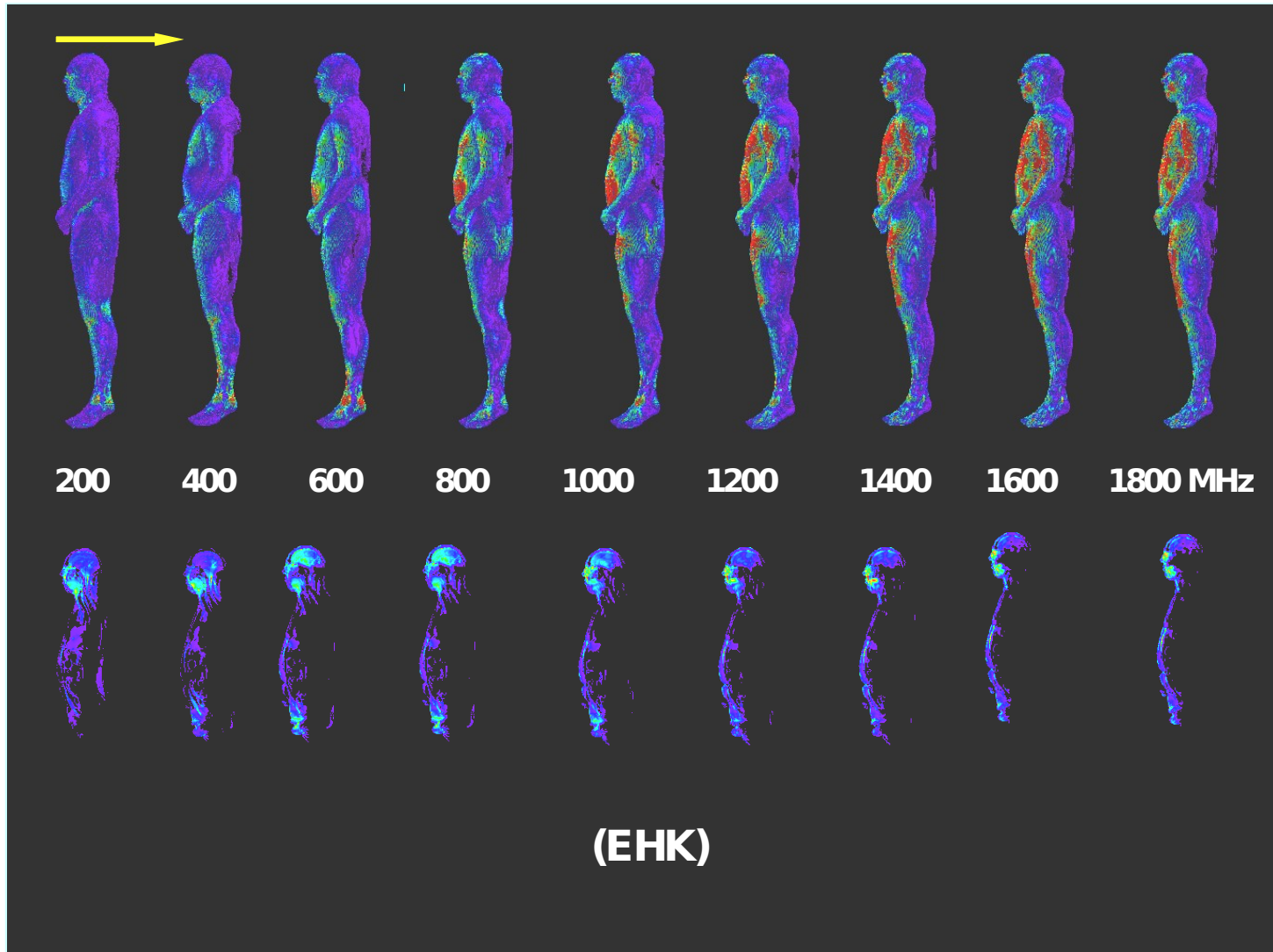


CD-1 female mice were initiated with 7,12-dimethylbenz[a] anthracene (DMBA). Some animals promoted with 12-O-tetradecanoylphorbol-13-acetate (TPA).

Exposed to 1.5 GHz, 0.084 W/kg, 90 min day, 5 days/week for 19 weeks.

RESULTS: No significant difference between exposed and control animals in terms of papilloma formation or squamous cell carcinoma formation.

Imaida *et al.* Lack of promotion of 7,12,-dimethylbenz[a] anthracene-initiated mouse skin carcinogenesis by 1.5 GHz electromagnetic near fields. *Carcinogenesis*, 22: 1837-1841, 2001.





PAVE PAWS CANCER STUDY?

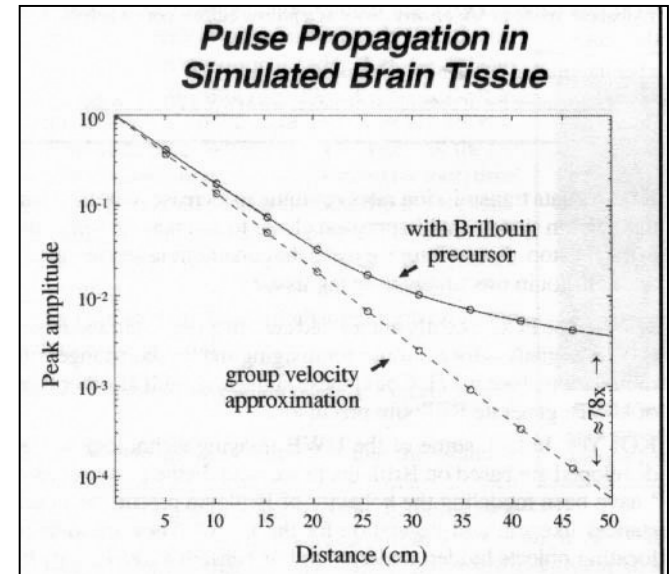


Precursors penetrate deeper into biological tissue than predicted for the “center” frequency by Beer’s Law.

Lower frequencies penetrate to a greater depth into biological tissue. Precursors result from the absorption of the higher frequency components and therefore have a lower energy level than the initial signal.

Phased array systems produce multiple signals within a short-time period.

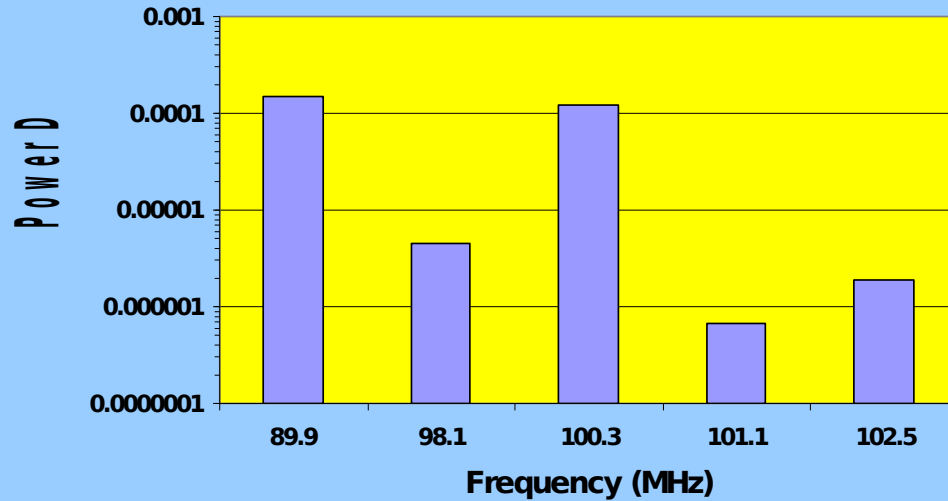
Multiple signals are produced by commercial communication



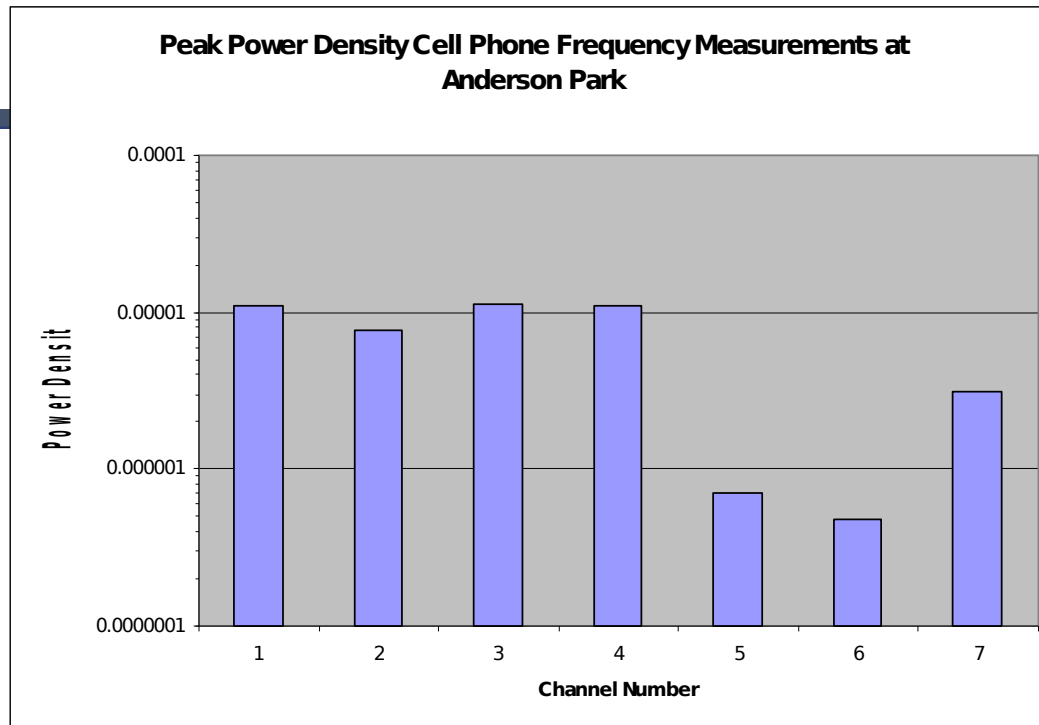
Dr. Kurt Oughstun



Peak Power Density - FM Radio Frequency Measurements at Anderson Park



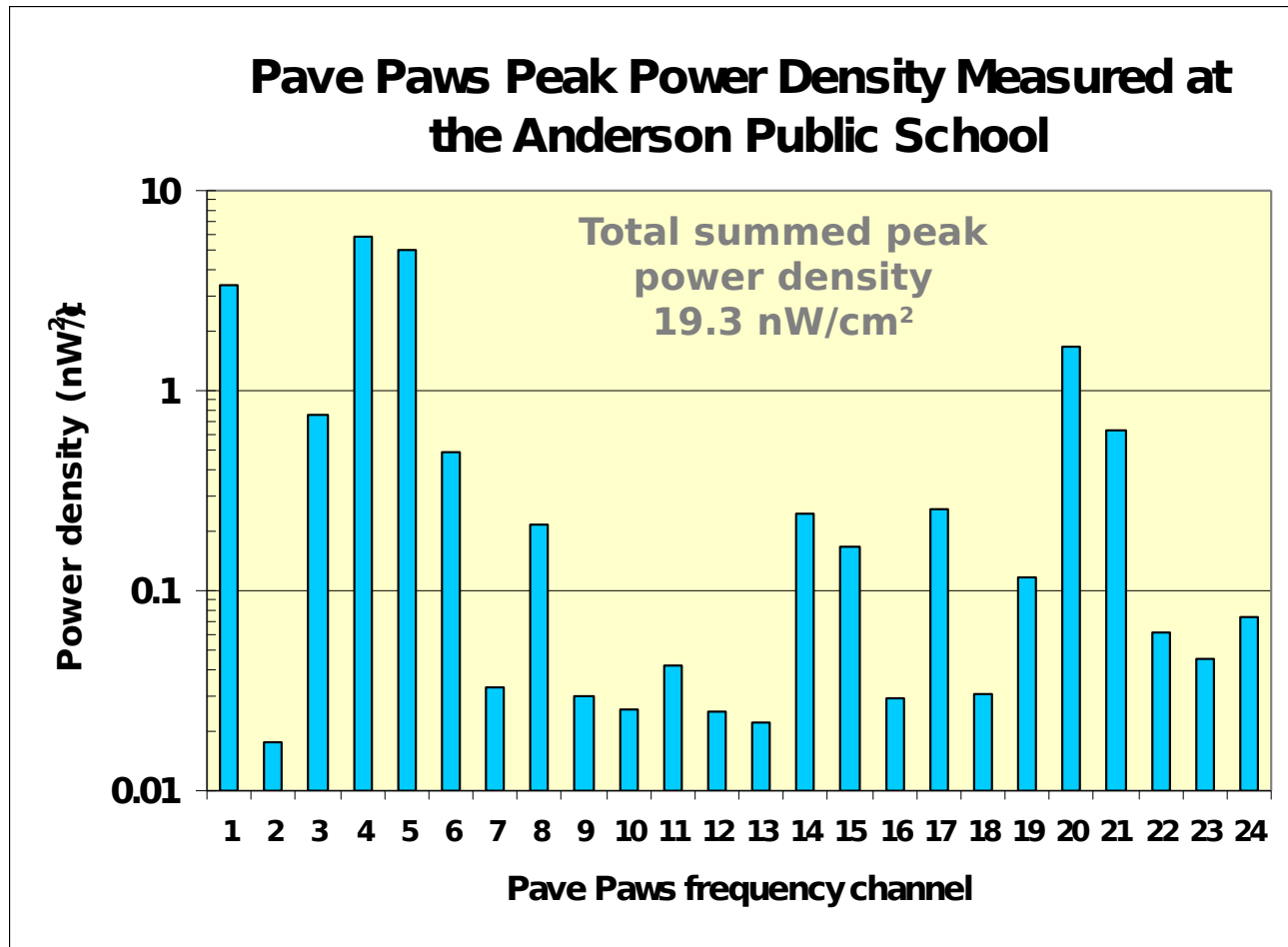
	Controlled	Uncontrolled	Measured	Fraction	Fraction
Frequency	MPE	MPE	Power Density	of	of
MHz	mW/cm2	mW/cm2	mW/cm2	Controlled	Uncontrolled
89.9	1.00	0.20	1.49E-10	1.49E-10	7.45E-10
98.1	1.00	0.20	4.57E-12	4.57E-12	2.28E-11
100.3	1.00	0.20	1.22E-10	1.22E-10	6.10E-10
101.1	1.00	0.20	6.60E-13	6.60E-13	3.30E-12
102.5	1.00	0.20	1.92E-12	1.92E-12	9.59E-12



	Controlled	Uncontrolled	Measured	Fraction	Fraction
Frequency	MPE	MPE	Power Density	of	of
MHz	mW/cm2	mW/cm2	mW/cm2	Controlled	Uncontrolled
879.39	2.93	0.59	1.09E-11	3.71E-12	1.86E-11
844.98	2.82	0.56	7.60E-12	2.70E-12	1.35E-11
879.99	2.93	0.59	1.14E-11	3.88E-12	1.94E-11
880.02	2.93	0.59	1.10E-11	3.77E-12	1.88E-11
880.62	2.94	0.59	6.95E-13	2.37E-13	1.18E-12
891.51	2.97	0.59	4.75E-13	1.60E-13	7.99E-13
893.97	2.98	0.60	3.14E-12	1.05E-12	5.27E-12



Representative Peak Power Densities at 3 Miles from Pave Paws, Anderson, Alaska





BRIEFING SUMMARY



Depth of energy absorption is a function of microwave frequency (greater penetration depth as the frequency decreases)

***In vivo* cancer studies have been conducted over a wide frequency range.**

Substantial body of scientific evidence indicating no significant relationship between microwave exposure (continuous or pulsed) and cancer.